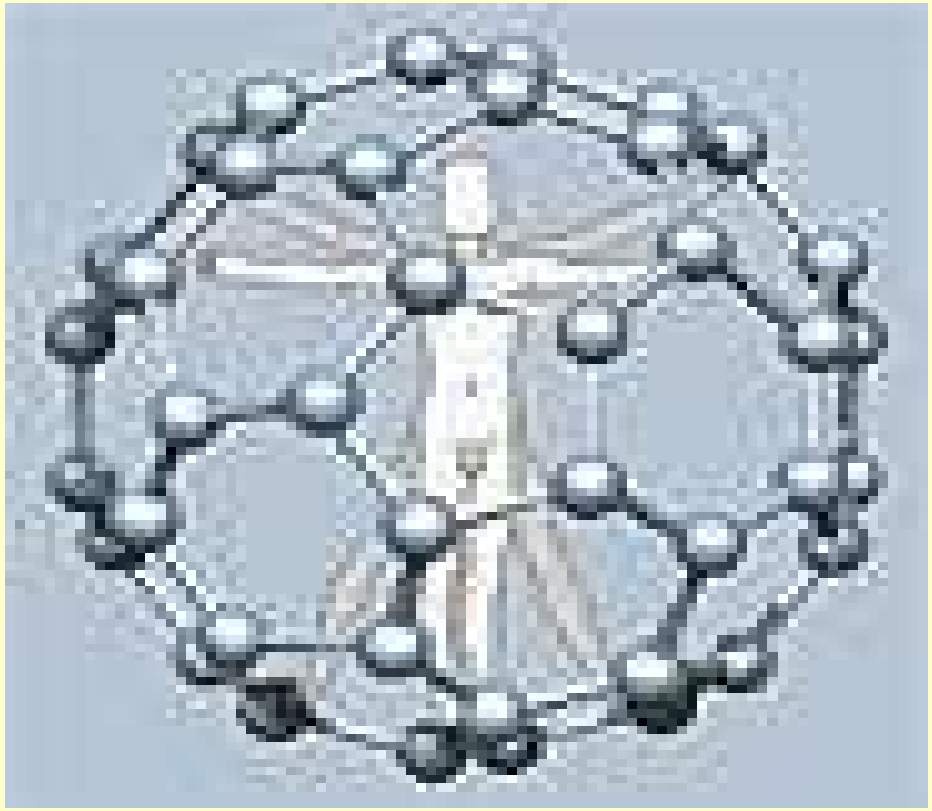
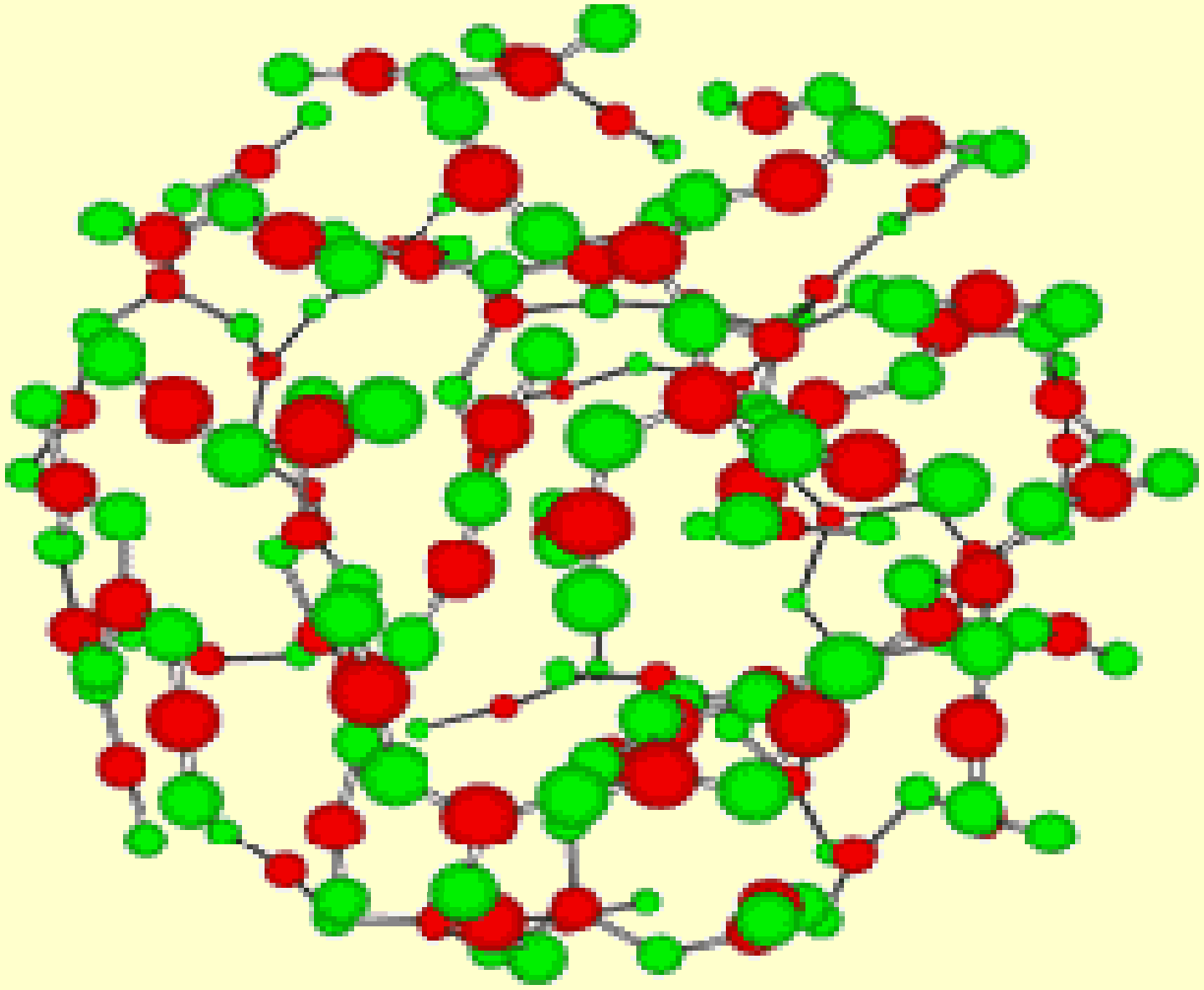
Helseeffekter av nanopartikler



Forum for miljøkartlegging og sanering
Oslo 7.2.2019

Bjørn Hilt
Arbeidsmedisinsk avdeling
St. Olavs hospital / NTNU
www.stolav.no/arbeidsmedisin



Forstørrelse: 500.000.000

Marked: 4,4 trillioner USD i 2018

National Nanotechnology Initiative (NNI):
95 % på produktutvikling
5 % på HMS

Kan utøve sin virkning både utapå og inni celler

Nanopartikler …definisjoner

- Nanopartikler = ultrafine partikler
- Nano = dverg
- Partikler < 100 nanometer diameter
- 1 nanometer = 10^{-9} meter
- 1 micrometer = 1000 nanometer
- Minste synlige partikkel:

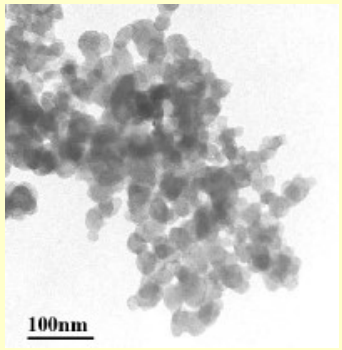
  ca 40 µm = 40.000 nanometer

Nanopartikler …karakteristika

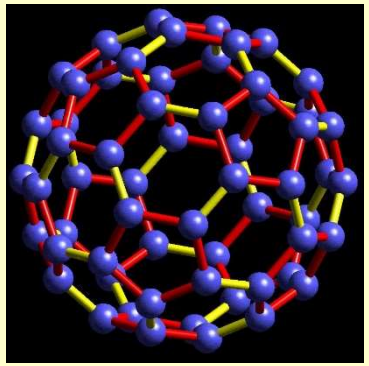
Sammenliknet med ”vanlige” partikler:

- Svært små
- Svært mange pr vektenhet
- Svært stor overflate pr vektenhet
- Fysiske karakteristika, risiko og helsefare er ofte forskjellig fra samme stoff med “normal” partikkelstørrelse

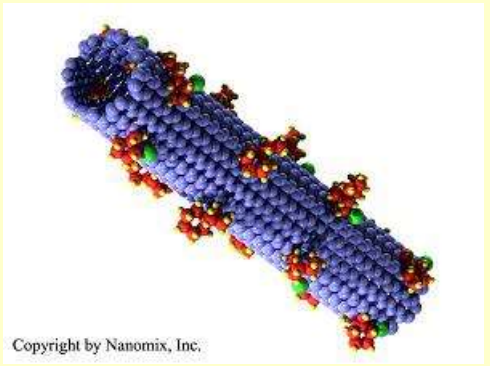
Nanopartikler …eksempler



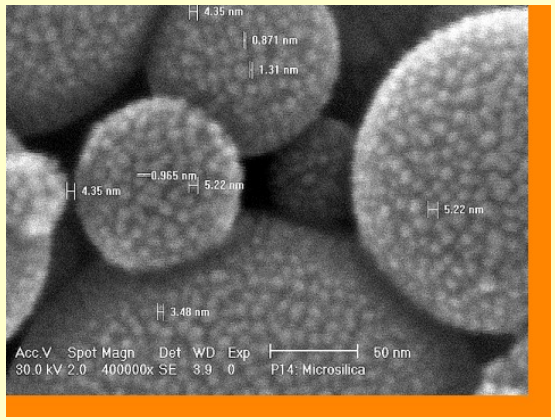
Dieseleksos



Buckyball



Nanorør

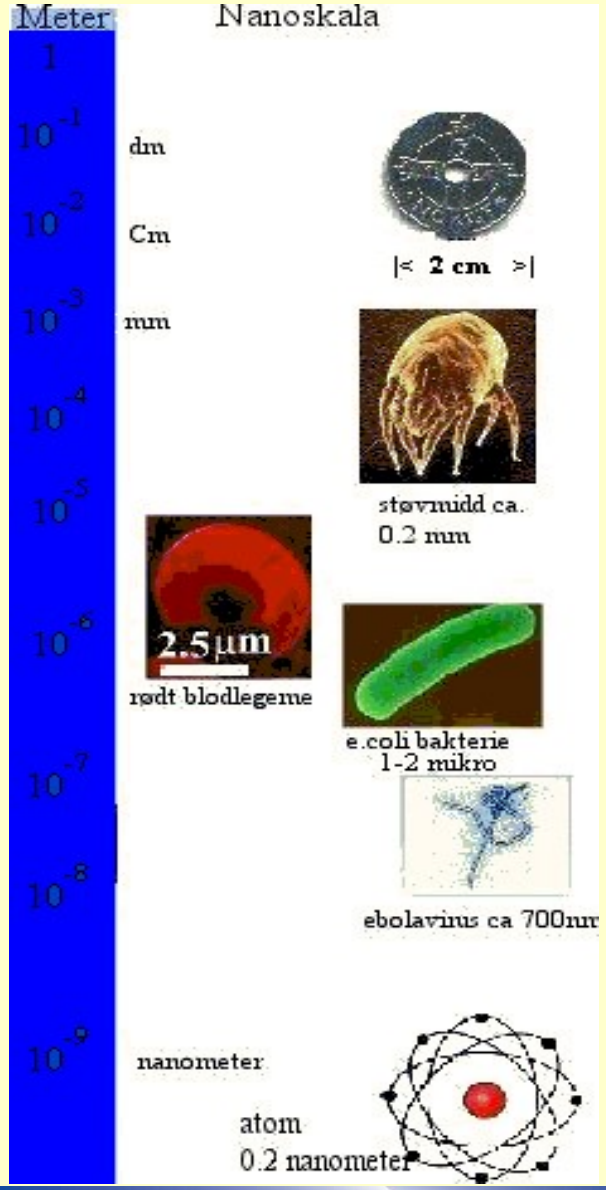


Microsilica

Sveiserøyk

Carbon black

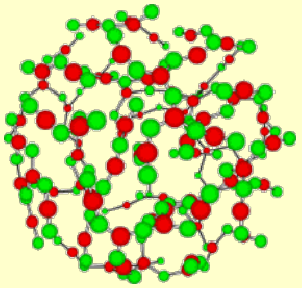
Nanopartikler ...definisjoner



Nanopartikler

12740 km

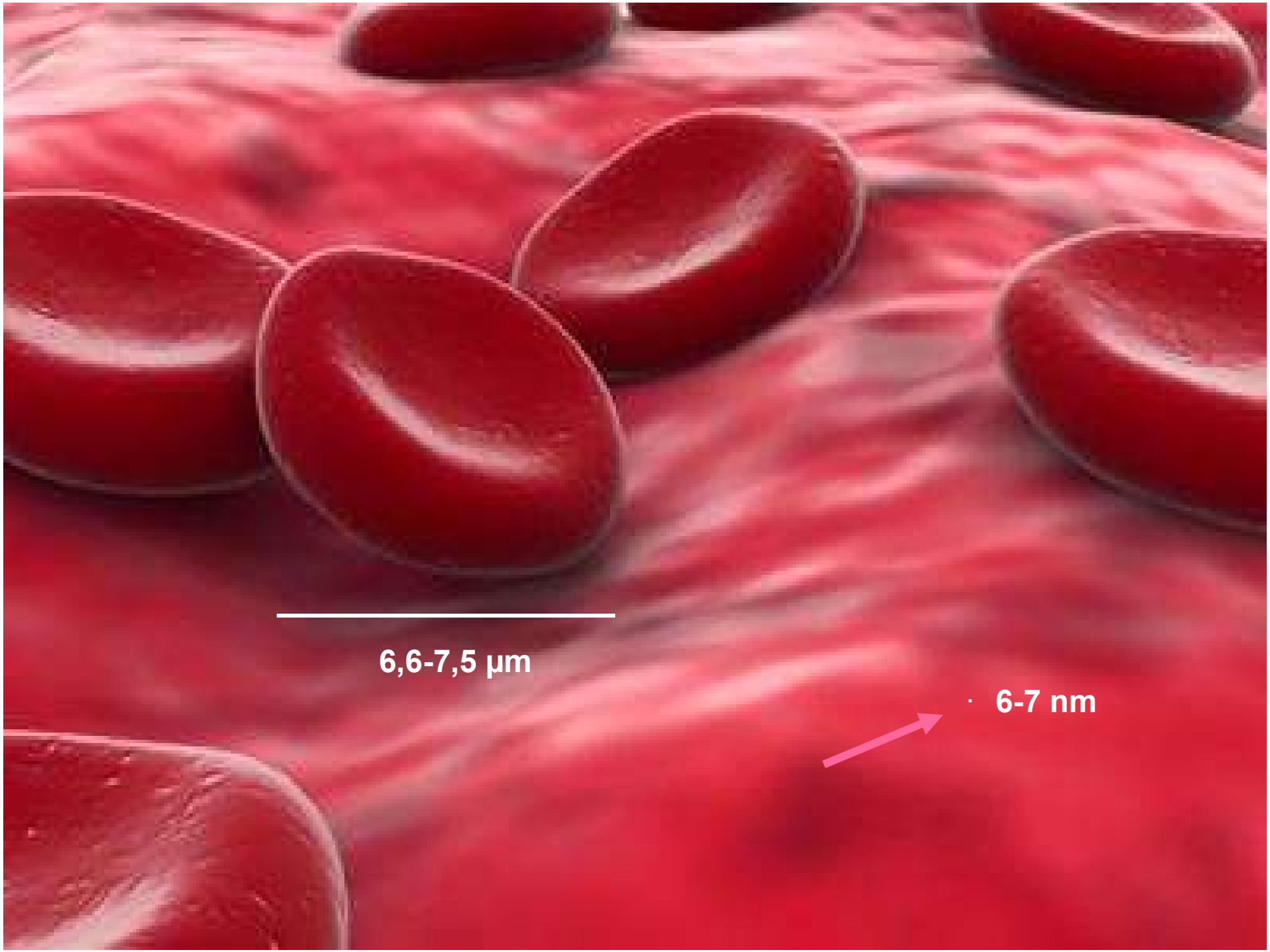
25 cm



5 nm

200.000.000	x	1	:	50.000.000

Ett hårstrå = 0,08 mm = 80 µm = 80.000 nm
HUMAN HAIR
20.000 nanopartikler får plass ved siden av hverandre innenfor Diameteren av et hårstrå


6,6-7,5 µm
6-7 nm

Number and surface area of monodisperse particles at an airborne concentration of 10 mg/m^3

Particle diameter (mm)	Number per ml of air	Particle surface (mm^2)
2	1.2	24
1	19	60
0.5	153	120
0.1	19 199	600
0.02	2 400 000	3 016

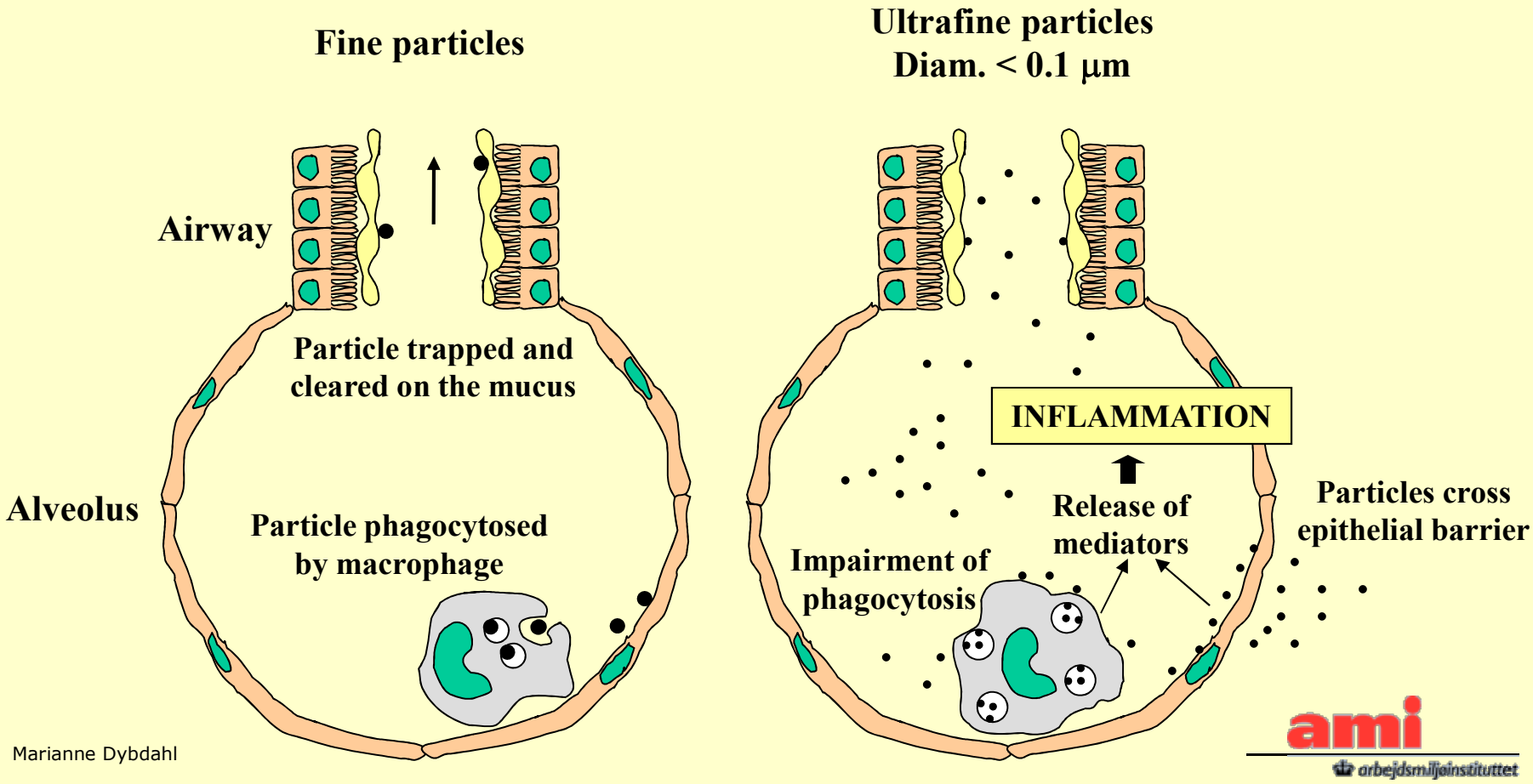
Nanopartikler har alltid vært i omgivelsene, som for eksempel i røyk fra forbrenning

Potensielle helseproblemer oppstår når vi begynner å lage tonnevis av partikler som vi tidligere kunne utsettes for noen gram av.

Mulige helseeffekter av nanopartikler

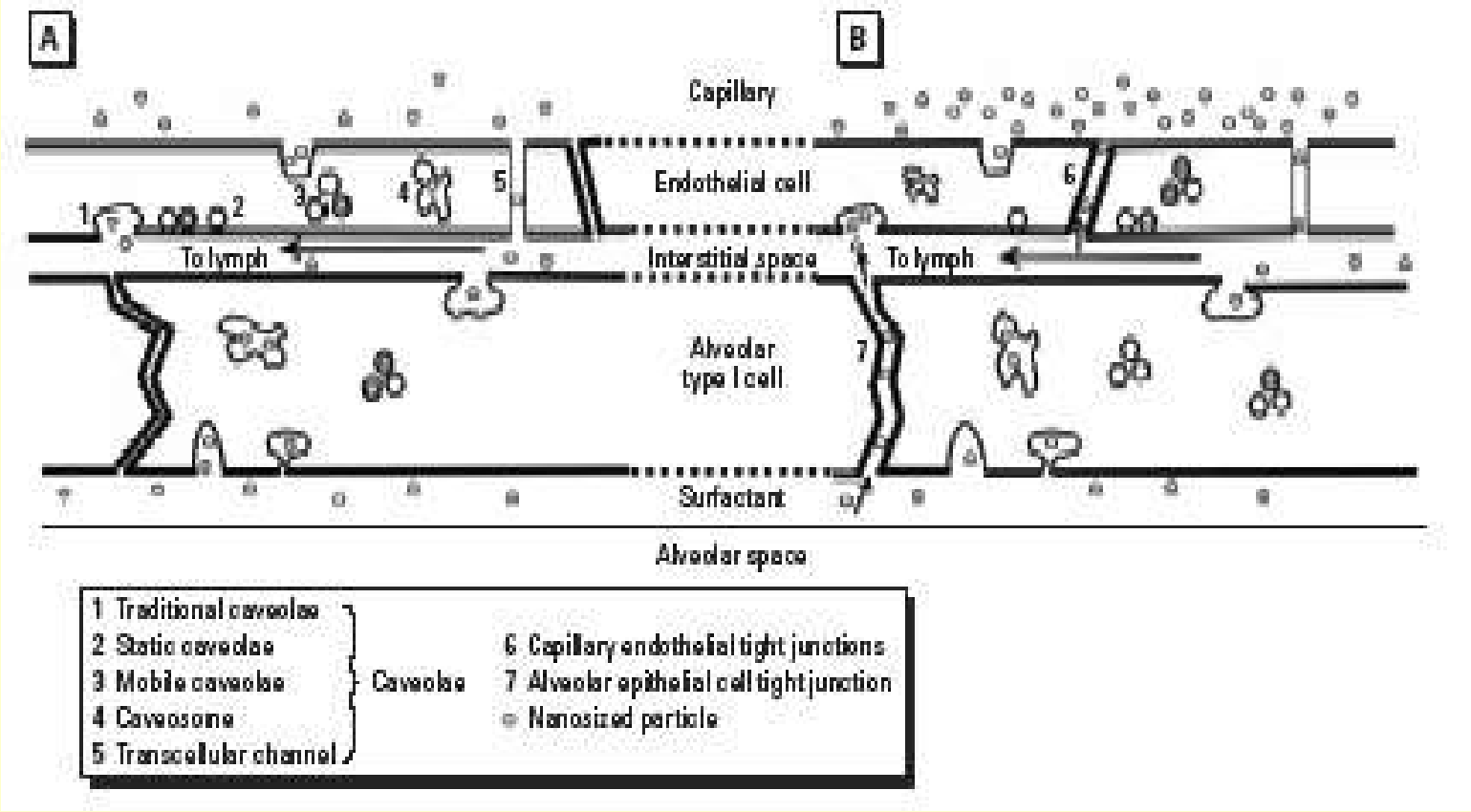
- Luftveiene
- Sentralnervesystemet
- Hjerte-karsykdommer
- Cellenivå
- ……

Hvad sker i lungen

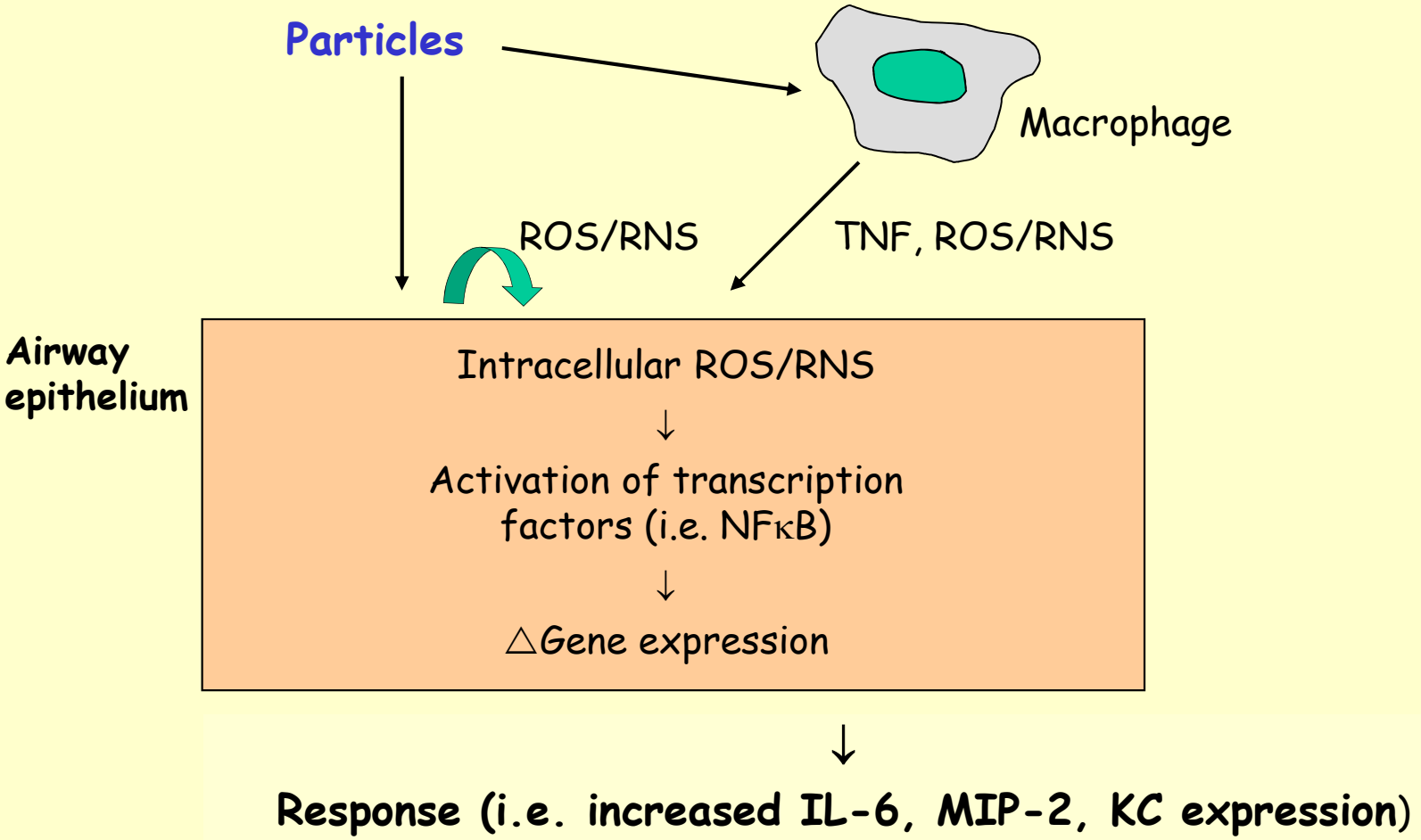


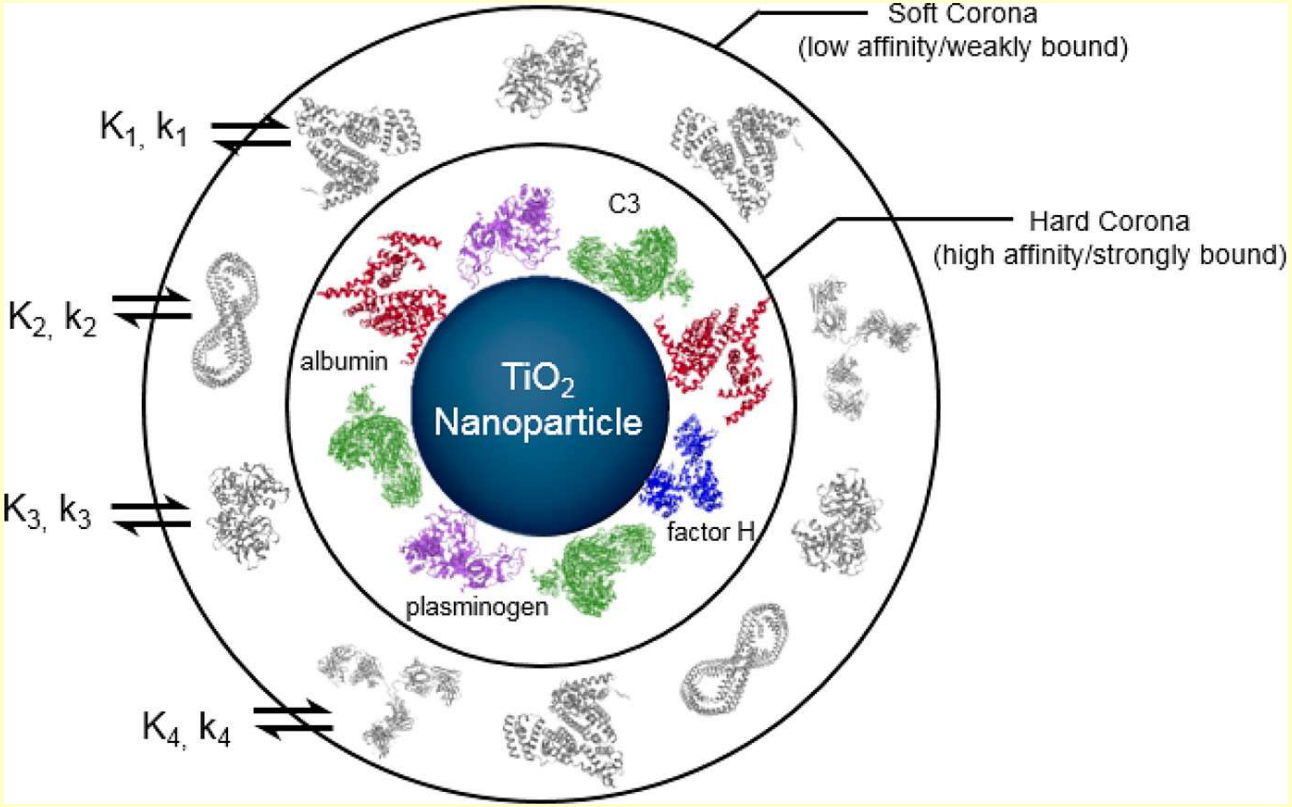
Marianne Dybdahl

Nanopartikler passerer membraner både mellom celler og gjennom celler



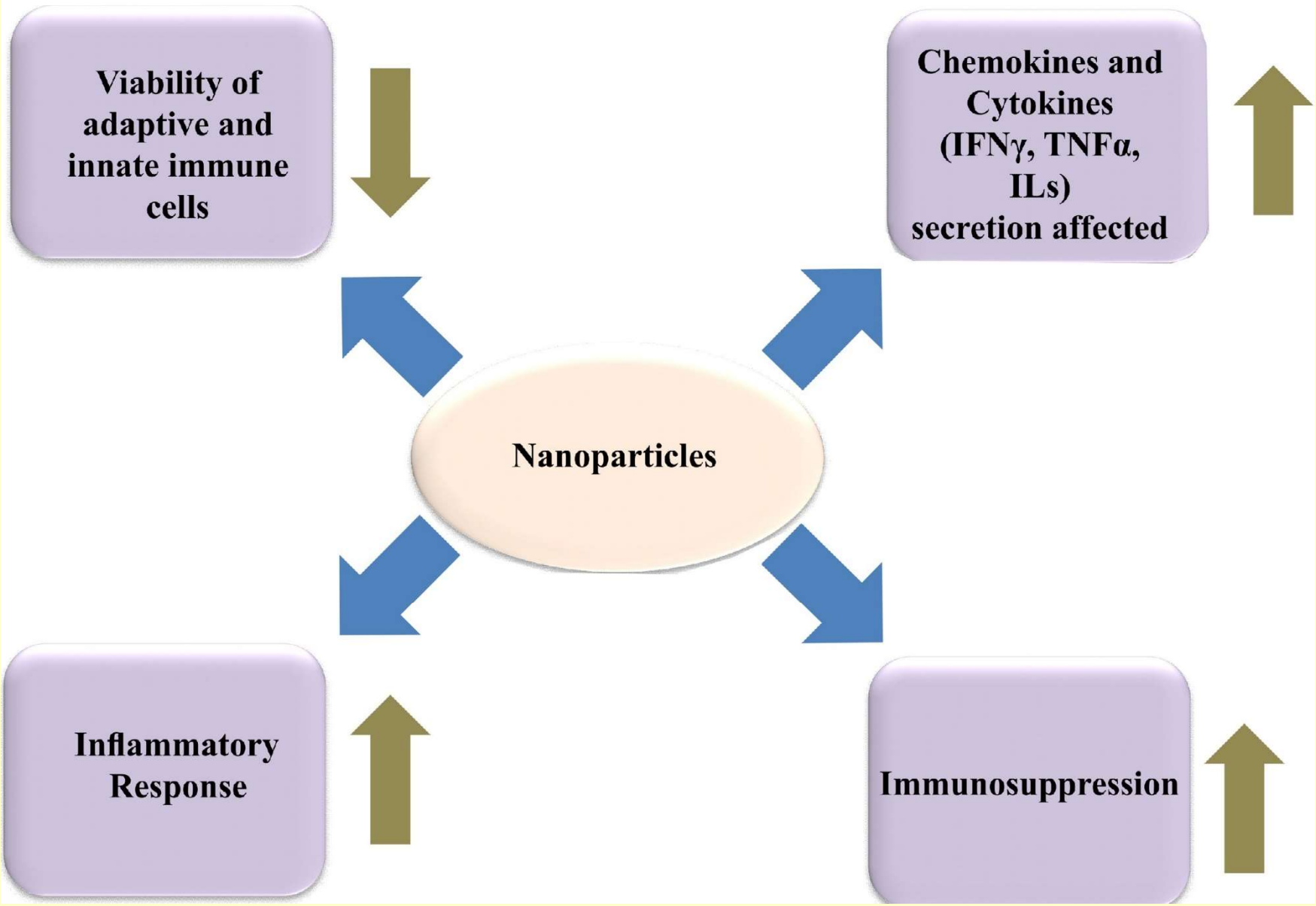
Respons i lungecellerne

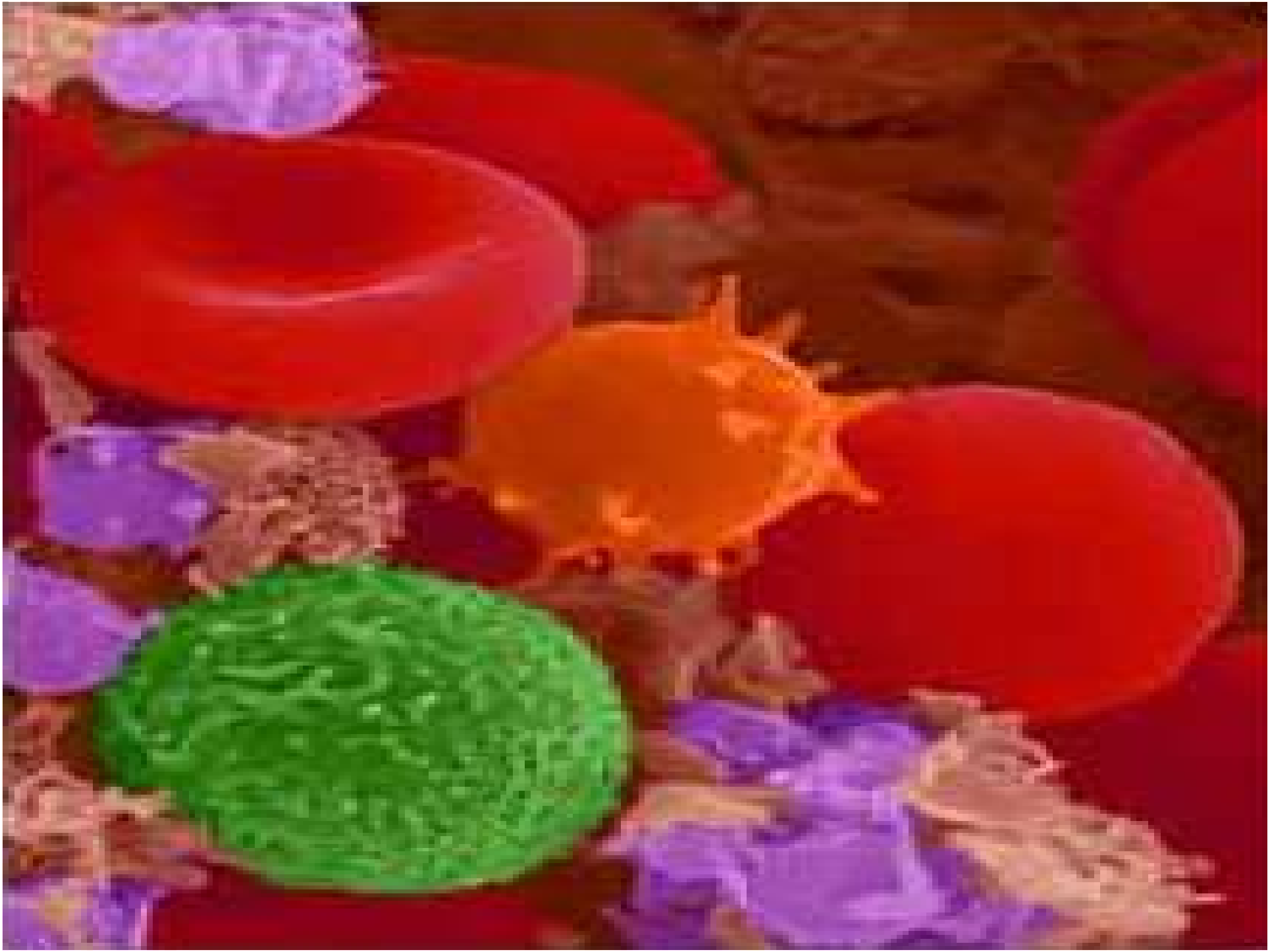


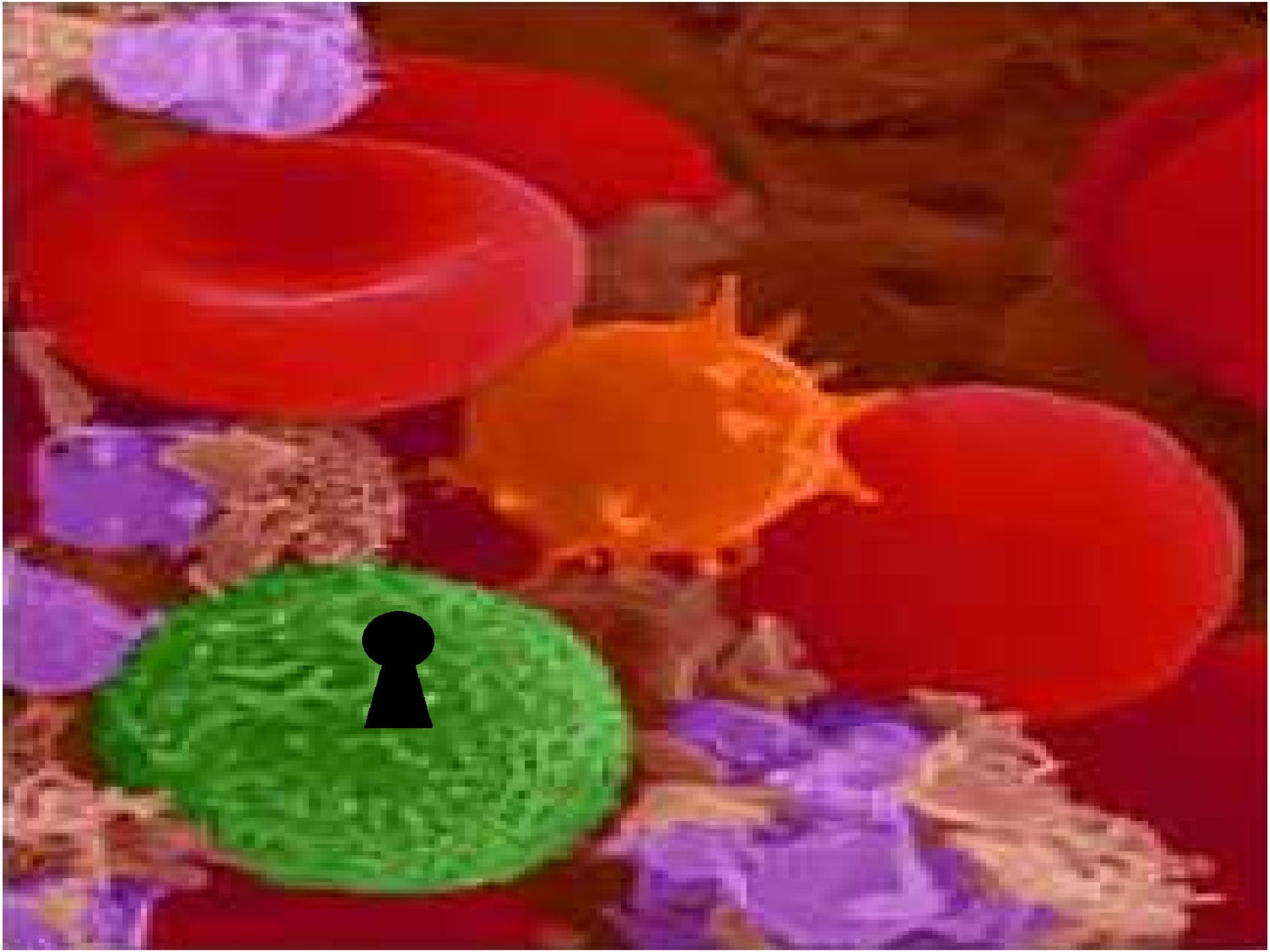


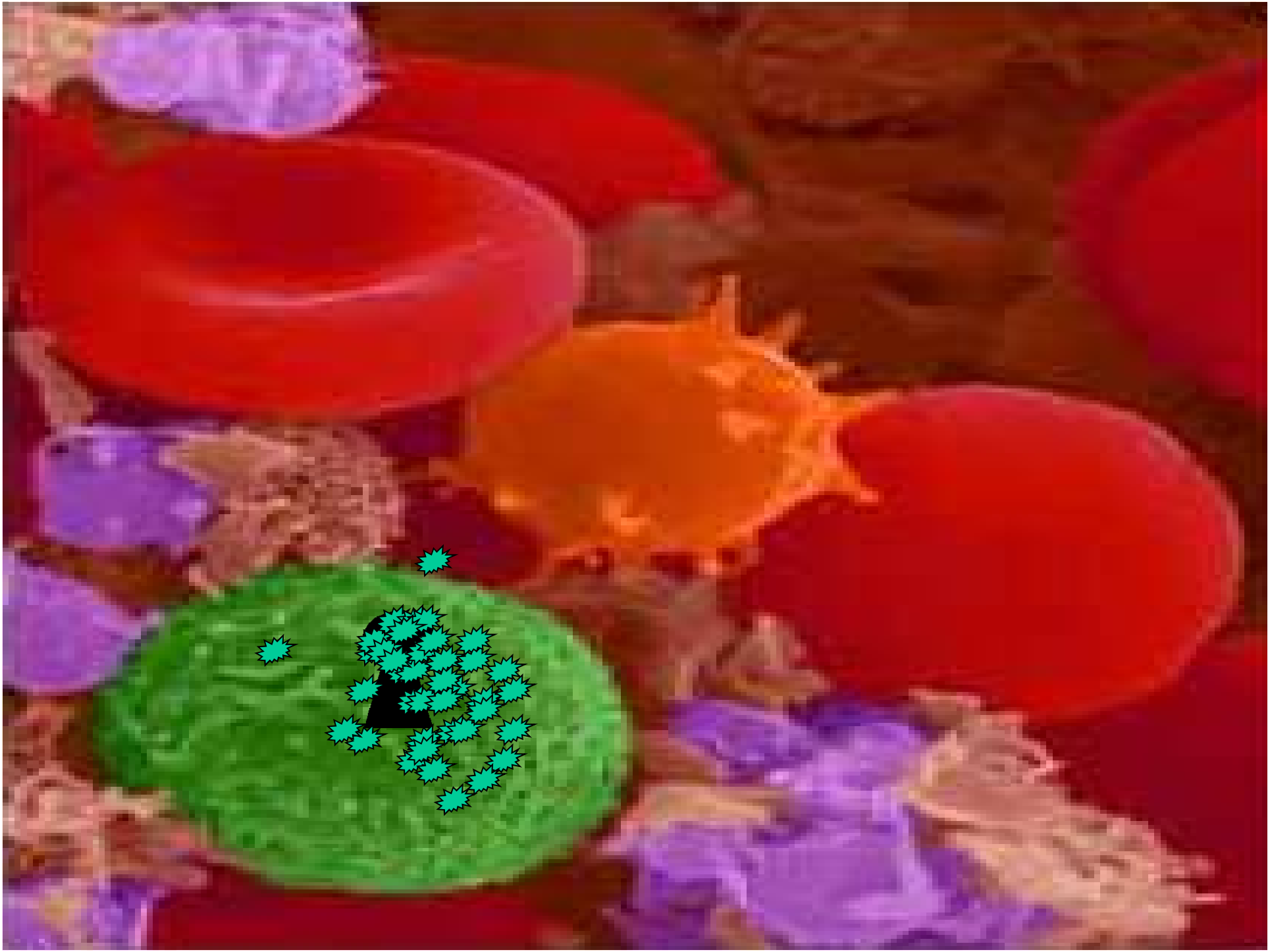
Schematic of the protein corona formed following incubation of TiO2 NPs with fetal bovine serum (FBS), a commonly used nutrient source for cells grown in culture. Proteins shown in the hard corona were the four most abundant proteins in the corona identified using mass spectrometry.(37) Soft corona proteins were not characterized in our experiments. Common serum proteins are shown in the schematic as an example. Protein structures were obtained from the Protein Data Bank. Adapted with permission from ref 32. Copyright 2014 American Chemical Society.

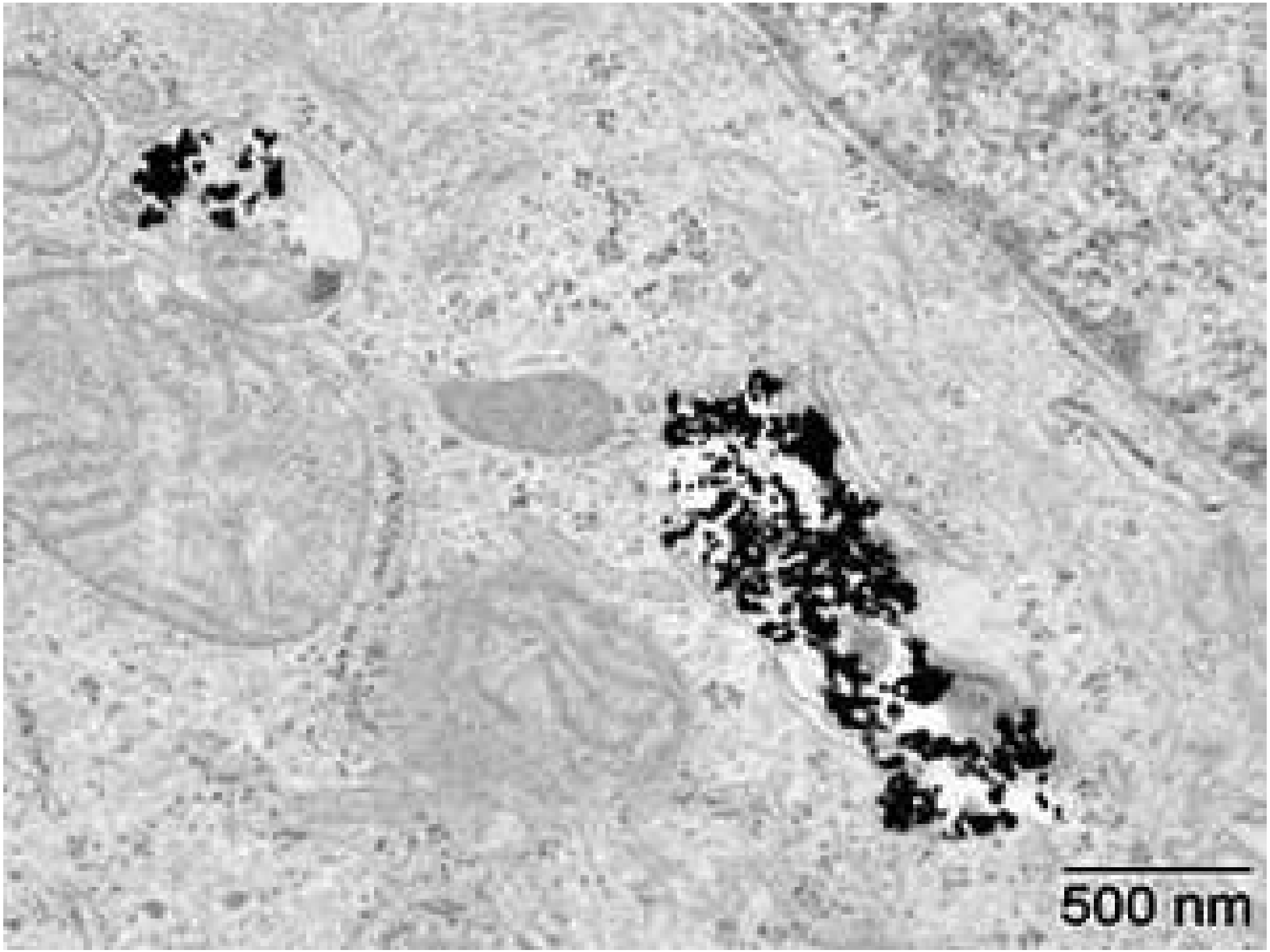
Published in: Sabiha Runa; Michael Hussey; Christine K. Payne; *J. Phys. Chem. B* **2018,** 122, 1009-1016.
DOI: 10.1021/acs.jpcb.7b08650
Copyright © 2017 American Chemical Society


Viability of adaptive and innate immune cells
Chemokines and Cytokines (IFNγ, TNFα, ILs) secretion affected
Nanoparticles
Inflammatory Response
Immunosuppression

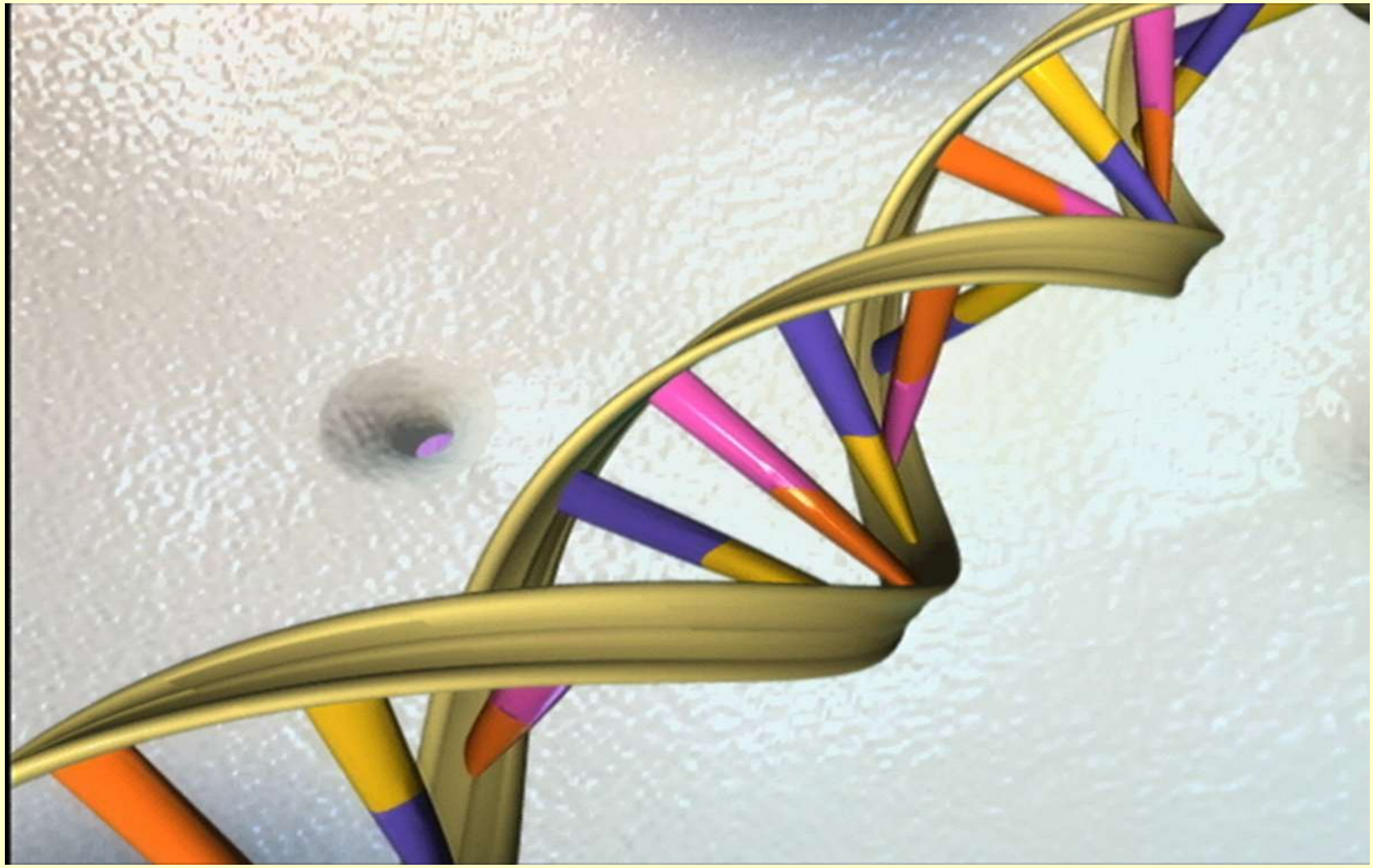







500 nm

Kan nanopartikler interferere med DNA?



Mulige effekter i sekundære målorgan:

- **Sentralnervesystemet:**
  - Via n. olfactorius
  - N. trigeminus
  - Sensoriske nerveendingar i tracheobronkial-regionen

  Aksonal (og dendrittisk?) transport

  Mulig mekanisme for Alzheimers sjukdom ???

- PNS ?

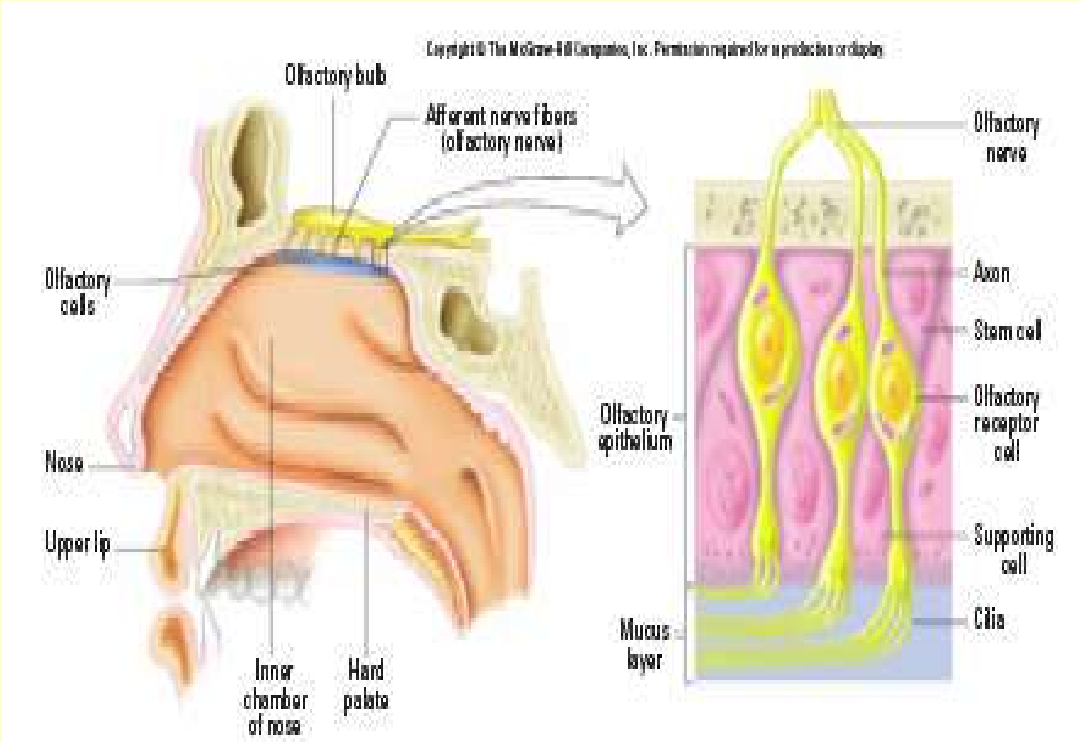
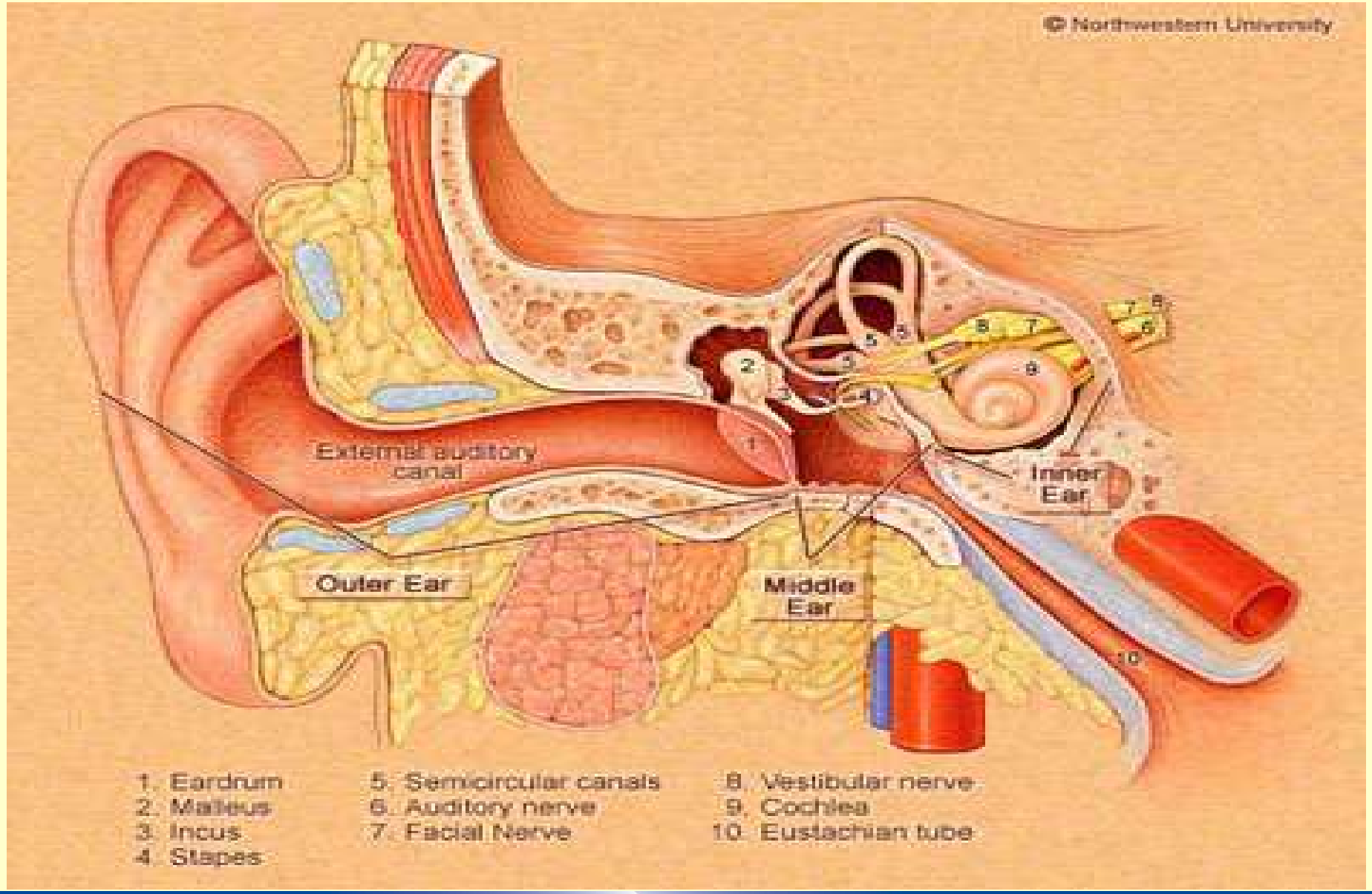
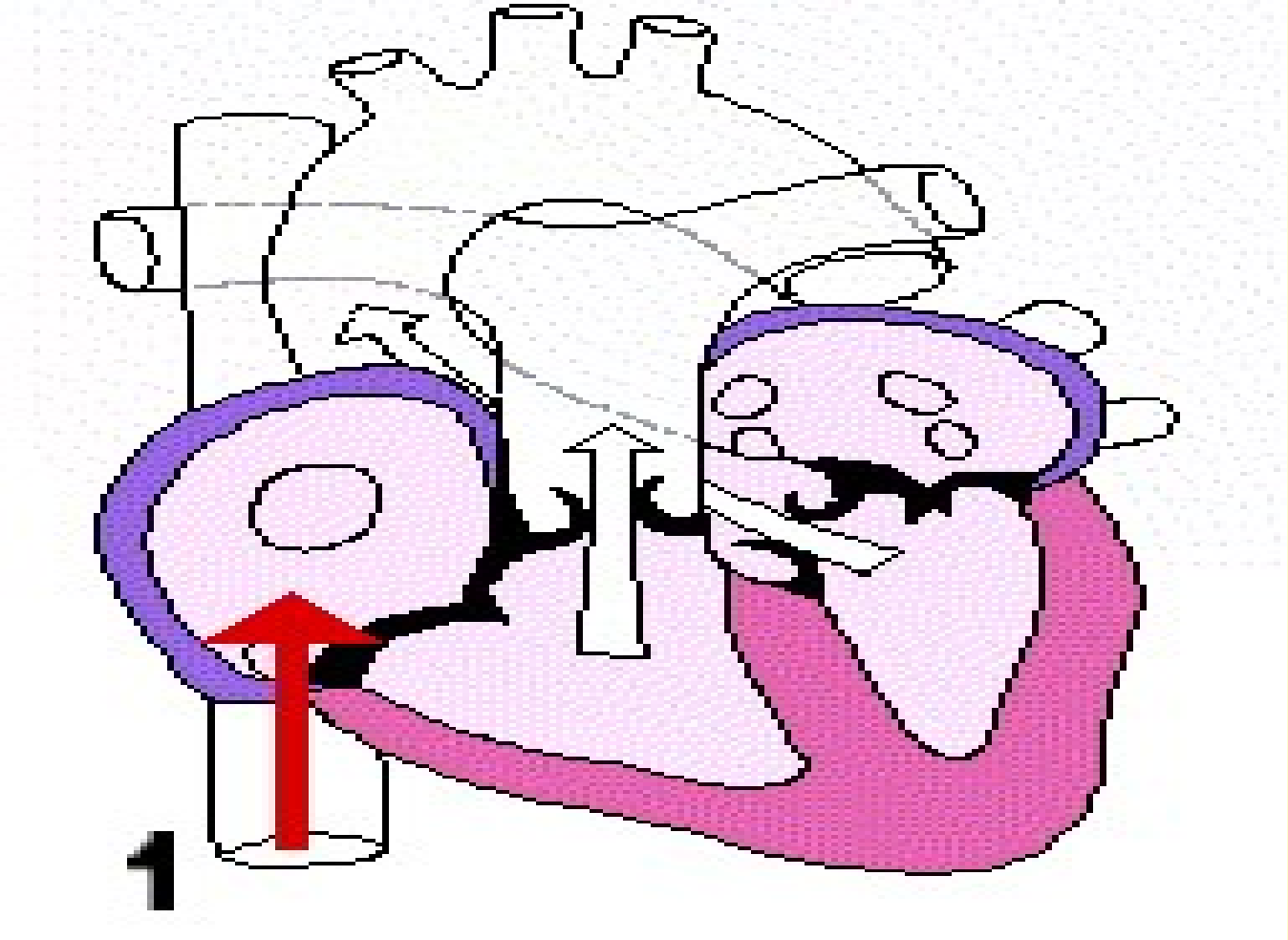


Figure 12. Close proximity of olfactory mucosa to olfactory bulb of the CNS. Inhaled NSP[s], especially below 10 nm, deposit efficiently on the olfactory mucosa by diffusion, similar to airborne "smell" molecules which deposit in this area of olfactory dendritic cilia. Subsequent uptake and translocation of solid NSP[s] along axons of the olfactory nerve has been demonstrated in non-human primates and rodents. Surface chemistry of the particles may influence their neuronal translocation. Copyright © the McGraw-Hill Companies, Inc. Reproduced from Widmaier et al. (2004) with permission from McGraw-Hill.

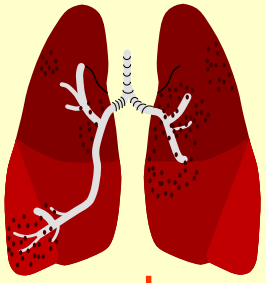
Mulige effekter i sekundære målorgan:



Kan nanopartikler forårsage hjertekarsygelighed?



Respirabelt støv
og nanopartikler

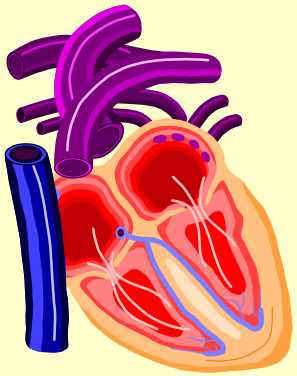


IL-6

Akuttfasereaksjoner
-Neutrofile celler
-CRP
-Alfa-1-antitrypsin

Fibrinogen

(D-dimer)



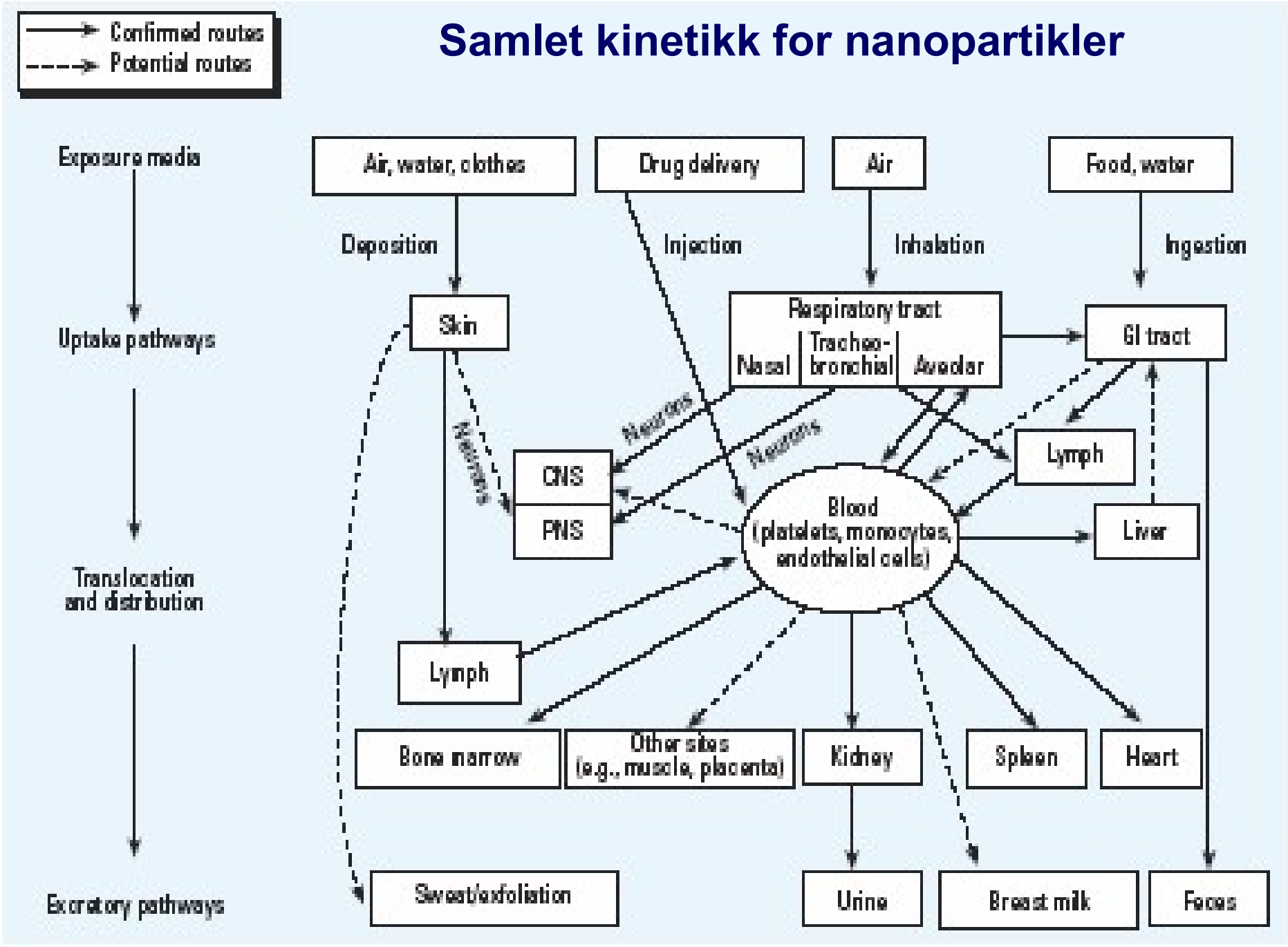
IHD

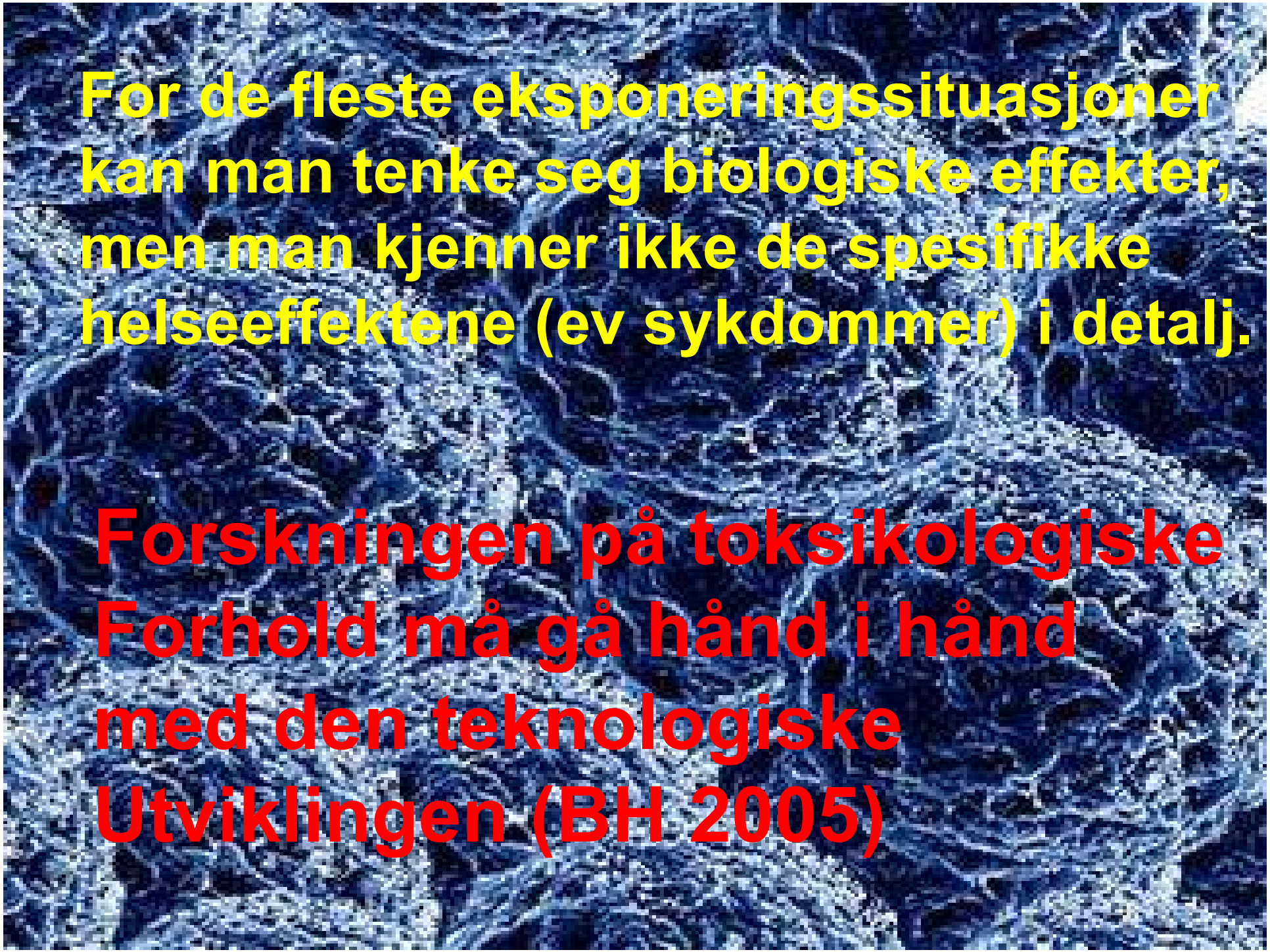
Helikobakter pylori
Chlamydia pneumoniae
Reumatoid artritt

Alder
Røyking
Diabetes mellitus
Høyt blodtrykk
Høyt LDL

Flere undersøkelser har vist økt forekomst av hjerteinfarkt etter episoder med smog eller annen luftforurensing

Samlet kinetikk for nanopartikler




For de fleste eksponeringssituasjoner kan man tenke seg biologiske effekter, men man kjenner ikke de spesifikke helseeffektene (ev sykdommer) i detalj.
Forskningen på toksikologiske Forhold må gå hånd i hånd med den teknologiske Utviklingen (BH 2005)

Box 1. Occupational activities with substantial probability of worker exposure to ENPs

- Construction (e.g. products improving wear resistance and insulation materials)
- Health care (e.g. drug-delivery systems and tissue engineering)
- Energy (e.g. low-wastage storage of energy and new generation photovoltaic cells)
- Automobile and aerospace industry (e.g. reinforced and stronger materials and fuel additives
- Chemical industry (e.g. catalysts and self-cleaning surfaces)
- Electronics and communication (e.g. optical/optoelectronic components and ultra fast compact computers)

Box 2. ENPs that have relevance in the workplace

- Single-walled carbon nanotubes
- Multi-walled carbon nanotubes
- Fullerene
- Carbon black
- Aluminium oxide
- Dendrimers
- Titanium dioxide, TiO_2
- Zinc oxide
- Cerium oxide
- Iron
- Silver
- Gold
- Layered silicates (nanoclays)
- Silicon dioxide

Table 1. Proposed workplace exposure limits for different ENPs (all data refer to concentration per cubic metre, when not otherwise specified)

ENPs	BSI (UK)	IFA (Germany)	DMSAE (The Netherlands)	NIOSH (USA)	SWA (Australia)	AIST (Japan)	KML (Korea)
Fibre-like ENPs							
Rigid, biopersistent CNTs	10^4 f	10^4 f	10^4 f	0.007 mg	10^5 f	0.03 mg	
Fibre-like metal oxides	10^4 f				10^5 f		
CNTs with explicitly excluded asbestos-like effects		4×10^7 p	4×10^7 p				
Biopersistent granular ENPs with a density <6000 kg/m³							
Titanium dioxide	0.066× WEL*	4×10^7 p	4×10^7 p	0.3 mg	0.03× Australian inhalable or 0.1× Australian respirable WEL	0.61 mg	
Carbon black	0.066× WEL* or 2×10^7 p	4×10^7 p	4×10^7 p		3 mg		3.5 mg
Silica	0.066× WEL* or 2×10^7 p	4×10^7 p	4×10^7 p		2 mg (fumed silica)		
Fullerene	0.066× WEL* or 2×10^7 p	4 x 10^7 p	4 x 10^7 p		0.03× Australian inhalable or 0.1× Australian respirable WEL	0.39 mg	
Zinc oxide, aluminium oxide, dendrimers, polystyrene, nanoclay	0.066× WEL* or 2×10^7 p	4×10^7 p	4×10^7 p		0.03× Australian inhalable or 0.1× Australian respirable WEL		
Biopersistent granular ENPs with a density >6000 kg/m³							
Cerium oxide, gold, iron, iron oxide, silver, cobalt, lanthane, lead, antimony oxide, tin oxide	0.066× WEL* or 2×10^7 p	2×10^7 p	2×10^7 p		0.03× Australian inhalable or 0.1× Australian respirable WEL		
Insoluble ENPs for which WEL* is not available					0.3 mg		
CMAR ENPs							
Nickel, cadmium containing quantum dots, chromium VI	0.1× WEL*	2×10^7 p	2×10^7 p		0.1× WEL*		
Beryllium, arsenic, zinc chromate	0.1× WEL*	4×10^7 p	4×10^7 p		0.1× WEL*		
CMAR ENPs for which WEL* is not available					0.003 mg		
Liquid and soluble ENPs							
Fat, hydrocarbons, syloxane		Same WEL*	Same WEL*				
Sodium chloride	0.5× WEL*	Same WEL*	Same WEL*		0.5× WEL*		
Other soluble ENPs	0.5× WEL*	Same WEL*	Same WEL*		0.5× WEL*		
Soluble ENPs for which WEL* is not available					1.5 mg		

f, fibres; p, particles; WEL*, work exposure limit of coarse material.

Box 4. Strategy for utilization of the available OELs

A. Company's control limits, if they are more stringent than other proposed regulatory limits.
B. National workplace exposure limits, if available.
C. Workplace exposure limits released by another country.
D. Proposed workplace exposure limits derived from research results.
E. Benchmark exposure levels which have some consideration of health effects.
F. Local particle reference values derived from characterizing background particle levels.